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TECH CENTER 1600/2900

ISPH-0576

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of

Lex M. Cowser et al

Appln. No. 09/854,883

Filed: May 14, 2001

For: ANTISENSE MODULATION OF PTP1B
EXPRESSION

) Group Art Unit: 1645

) Examiner:

#5/K.T.
10/4

Revoc.
w/ P.O.A

Assistant Commissioner for Patents
Washington, DC 20231

**POWER OF ATTORNEY BY ASSIGNEE OF ENTIRE INTEREST AND
REVOCATION OF PRIOR POWERS**

Sir:

As assignee of record of the entire interest of the above-identified application, ISIS PHARMACEUTICALS, INC. hereby revokes all powers of attorney previously given.

ISIS PHARMACEUTICALS, INC. hereby appoints the following attorney(s) and/or agent(s) to prosecute and transact all business in the U. S. Patent and Trademark Office connected with the above-identified application: Stanley B. Kita, Registration No. 24,561; George A. Smith, Jr., Registration No. 24,442; Mary E. Bak, Registration No. 31,215; Cathy A. Kodroff, Registration Number 33,980;

CERTIFICATE UNDER 37 CFR §1.8(a)

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: the Assistant Commissioner for Patents, Washington, DC 20231 on 9-18-2001

Signature

Typed or printed name

Debra N. Gerstemeier

William Bak, Registration Number 37,277; Tracy U. Palovich, Registration No. 47,840 (patent agent), all of the firm of HOWSON AND HOWSON, of Spring House, Pennsylvania; and Herb Boswell, Registration No. 27,311; Laurel S. Bernstein, Registration No. 37,280; April Logan, Registration No. 33,950; and Neil S. Bartfeld, Registration No. 39,901, all of ISIS PHARMACEUTICALS, INC., of Carlsbad, California.

Address all telephone calls to Mary E. Bak at telephone no. (215) 540-9206. Address all correspondence to HOWSON AND HOWSON, Spring House Corporate Center, Box 457, Spring House, Pennsylvania 19477.

ISIS PHARMACEUTICALS, INC. certifies that it is the assignee of the entire right, title and interest in the patent application identified above by virtue of an assignment from the inventors.

The evidentiary documents relating to the ownership of the above-identified application and the invention claimed therein have been reviewed, and consist of an assignment of the above-identified U. S. Patent Application No. 09/854,883 from the inventors to ISIS Pharmaceuticals, Inc. A copy of the assignment from the inventors to ISIS Pharmaceuticals, Inc. is attached hereto and the original of said assignment was forwarded to the U. S. Patent and Trademark Office for recordation.

The undersigned has reviewed all the documents in the chain of title of the patent application identified above, and, to the best of undersigned's knowledge and belief, title is in the assignee identified above.

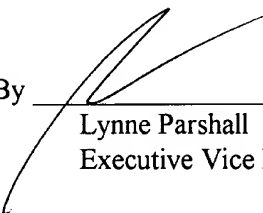
The undersigned is empowered to sign this certificate on behalf of the assignee. To the best of the undersigned's knowledge and belief, title is solely in the assignee ISIS Pharmaceuticals, Inc.

I hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, or any patent issuing thereon.

ISIS PHARMACEUTICALS, INC.

Date SEPT, 04, 2001

By


Lynne Parshall
Executive Vice President

Enclosures:

- (1) Copy of Assignment from inventors to ISIS Pharmaceuticals, Inc.

A S S I G N M E N T

WHEREAS, We, Lex M. Cowser, of San Mateo, State of California; Jacqueline Wyatt, of Encinitas, State of California; Susan M. Freier, of San Diego, State of California; Brett P. Monia, of ~~La Costa~~ ^{ENCINITAS}, State of California; Madeline M. Butler, of Rancho Santa Fe, State of California and Robert McKay, of San Diego, State of California, have invented a certain invention entitled Antisense Modulation of PTP1b Expression, for which we have made application for Letters Patent of the United States, said application having been filed May 14, 2001 and assigned Application No. 09/854,883; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

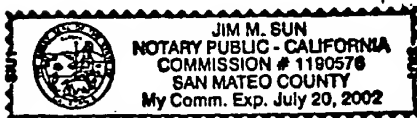
DATED: 7/30, 2001


Lex M. Cowser

State of California)
)
County of San MATEO) ss.
)
County of San Diego)

On this 30TH day of JULY, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowser, ~~personally known to me~~ proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.




Signature of Notary

DATED: _____, 2001

Jacqueline Wyatt

State of California)
) ss.
County of San Diego)

On this _____ day of _____, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Jacqueline Wyatt, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Signature of Notary

DATED: _____, 2001

Susan M. Freier

State of California)
) ss.
County of San Diego)

On this _____ day of _____, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Susan M. Freier, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Signature of Notary

DATED: _____, 2001

Brett P. Monia

State of California)
) ss.
County of San Diego)

On this _____ day of _____, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Signature of Notary

DATED: _____, 2001

Madeline M. Butler

State of California)
) ss.
County of San Diego)

On this _____ day of _____, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Signature of Notary

DOCKET NO.: ISPH-0576

PATENT

DATED: _____, 2001

Robert McKay

State of California)
) ss.
County of San Diego)

On this _____ day of _____, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Robert McKay, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Signature of Notary

A S S I G N M E N T

WHEREAS, We, Lex M. Cowsert, of San Mateo, State of California; Jacqueline Wyatt, of Encinitas, State of California; Susan M. Freier, of San Diego, State of California; Brett P. Monia, of ^{ENCINITAS}~~La Costa~~, State of California; Madeline M. Butler, of Rancho Santa Fe, State of California and Robert McKay, of San Diego, State of California, have invented a certain invention entitled Antisense Modulation of PTP1b Expression, for which we have made application for Letters Patent of the United States, said application having been filed May 14, 2001 and assigned Application No. 09/854,883; and

WHEREAS, ISIS Pharmaceuticals, Inc. hereinafter referred to as the assignee, of 2292 Faraday Avenue, Carlsbad CA, a corporation of Delaware, is desirous of acquiring the entire right, title and interest in and to the said inventions or improvements and in and to the said application, and in, to and under any and all Letters Patent which may be granted on or as a result thereof in any and all countries:

NOW, THEREFORE, for and in consideration of the sum of One Dollar (\$1.00) to each of us in hand paid by said assignee, and other good and valuable consideration, the receipt of which is hereby acknowledged, we, the said assignors, have sold, assigned, transferred and set over, and by these presents do hereby sell, assign, transfer and set over to said assignee, the entire right, title and interest in and to said inventions or improvements and said application and any and all continuations, divisions and renewals of and substitutes for said application, and in, to and under any and all Letters Patent which may be granted on or as a

result thereof in the United States and any and all other countries, and any reissue or reissues or extension or extensions of said Letters Patent, and assign to and authorize said assignee, to file in our names applications for Letters Patent in all countries, the same to be held and enjoyed by said assignee, its successors, assigns, nominees or legal representatives, to the full end of the term or terms for which said Letters Patent respectively may be granted, reissued or extended, as fully and entirely as the same would have been held and enjoyed by us had this assignment, sale and transfer not been made.

AND we hereby covenant that we have full right to convey the entire interest herein assigned, and that we have not executed and will not execute any agreement in conflict herewith, and we further covenant and agree that we will each time request is made and without undue delay, execute and deliver all such papers as may be necessary or desirable to perfect the title to said inventions or improvements, said application and said Letters Patent to said assignee, its successors, assigns, nominees, or legal representatives, and each of us agrees to communicate to said assignee or to its nominee all known facts respecting said inventions or improvements, said application and said Letters Patent, to testify in any legal proceedings, to sign all lawful papers to execute all disclaimers and divisional, continuing, reissue and foreign applications, to make all rightful oaths, and generally to do everything possible to aid said assignee, its successors, assigns, nominees and legal representatives to obtain and enforce for its or their own benefit proper patent protection for said inventions or improvements in any and all countries.

AND we hereby authorize and request the Commissioner of Patents and Trademarks of the United States and any official of any country or countries foreign to the United States whose duty it is to issue patents on applications as aforesaid, to issue to said assignee, as assignee of the entire right, title and interest, any and all Letters Patent for said inventions or improvements, including any and all Letters Patent of the United States which may be issued and granted on or as a result of the application aforesaid, in accordance with the terms of this assignment.

IN WITNESS WHEREOF, we have hereunto set our hands and seals.

DATED: _____, 2001

Lex M. Cowsert

State of California)
) ss.
County of San Diego)

On this _____ day of _____, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Lex M. Cowsert, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.

Signature of Notary

DATED: 4/15, 2001Jacqueline R Wyatt
Jacqueline Wyatt

State of California)
) ss.
 County of San Diego)

On this 19th day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Jacqueline Wyatt, personally known to me/proved to me on the basis of satisfactory evidence to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

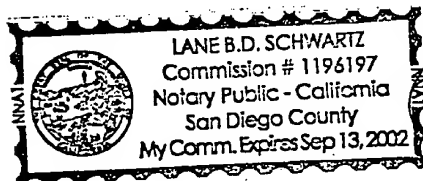
Pamela Groome
 Signature of Notary

DATED: July 30th, 2001

Susan M. Freier
 Susan M. Freier

State of California)
) ss.
 County of San Diego)

On this 30th day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Susan M. Freier, personally known to me/proved to me on the basis of ~~satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Lane B.D. Schwartz
 Signature of Notary

DATED: 7/31, 2001

Brett P. Monia
Brett P. Monia

State of California)
) ss.
County of San Diego)

On this 31st day of July, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Brett P. Monia, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



WITNESS my hand and official seal.

Lane B.D. Schwartz
Signature of Notary

DATED: 8/14, 2001

Madeline M. Butler
Madeline M. Butler

State of California)
) ss.
County of San Diego)

On this 14 day of August, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Madeline M. Butler, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that she executed the same in her authorized capacity, and that by her signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.



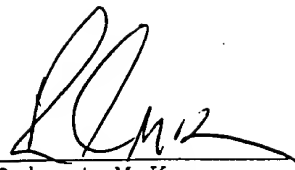
WITNESS my hand and official seal.

Lane B.D. Schwartz
Signature of Notary

DOCKET NO.: ISPH-0576

PATENT

DATED: 8-13-01, 2001

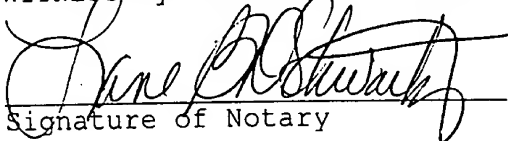

Robert McKay

State of California)
) ss.
County of San Diego)

On this 13th day of August, 2001, before me, the undersigned, a Notary Public for the state, personally appeared Robert McKay, personally known to me/~~proved to me on the basis of satisfactory evidence~~ to be the person who subscribed the foregoing Assignment and acknowledged to me that he executed the same in his authorized capacity, and that by his signature on the Assignment the person, or the entity on behalf of which the person acted, executed the Assignment.

WITNESS my hand and official seal.




Signature of Notary